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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/628,391	07/29/2003	Henry J. Windle	P69048US0	3959

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EXAMINER

PORTNER, VIRGINIA ALLEN

ART UNIT

PAPER NUMBER

1645

DATE MAILED: 05/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/628,391	WINDLE ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 3/10/2005
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 17-27 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17-27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Examined claims 1-16 have been canceled; all new claims 17-27 have been submitted.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections Withdrawn

1. All prior pending, examined claims have been canceled.

Response to Arguments

2. Applicant traverses the rejection of claim 27, under 35 USC 102(b), as previously applied to claims 1-7 and 15-16, directed to an isolated *Helicobacter pylori* thioredoxin protein, as being anticipated by either Tomb et al (1997) or Alm et al (1999) in light of evidence provided by Swiss-Prot accession number P56430, on the grounds that both Tomb et al and Alm et al disclose lists of genes in the bacterium and there is no disclosure or indication of the function of the genes described.

3. It is the position of the examiner that both Tomb et al and Alm et al, deposited the amino acid sequence for an isolated *H. pylori* protein into Swiss-Prot under accession number P56430, on July 1998, wherein the proteins' amino acid sequence shares 100% sequence identity with the instantly claimed isolated *H. pylori* thioredoxin protein. The biological function of the three dimensional protein is an inherent characteristic based upon the proteins amino acid sequence and the resultant folded structure based upon the amino acid sequence. Patentability of a known product is not permissible based upon a newly discovered function, but claims to a new use for a known product may be claimed as a method. Inherently the reference anticipates the now claimed invention. *Atlas Powder Co. V IRECA*, 51 USPQ2d 1943, (FED Cir. 1999) states Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art

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composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. The Court further held that this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art. Also see In re Crish 04-1075 The prior art rejection is maintained for reasons of record.

New Claims/New Claim Limitations/New Grounds of Objection/Rejection

Claim Objections

4. Claims 22 is objected to because of the following informalities:
5. New claim 22 recites the phrase “selected from the group consisting of” but sets forth the Markush group in an incorrect format : A or B, C, D, E, F, G and H.; the format should be A, B, C, D, E, F, G, and H. Appropriate correction is required.
6. Claim 24 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 24 recites the phrase “used in the preparation of a medicament” and depends from claim 17 which is directed to a method of treating and preventing inflammation by carrying out the step of “administering to a subject”. Claim 24 seeks to change the method claimed in claim 17 which administers a composition, into a method of preparing a medicament. Claim 24 is not further limiting of claim 17 from which it depends and does not set forth any additional methods steps.
7. Claims 19-24 are not further limiting of the base claim as they provide for the use of “The method as claimed in claim 17 used”, but, since the dependent claims do not set forth any additional steps involved in the method/process of claim 17, ^{they} ~~and~~ are not further limiting of the

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administering step recited in claim 17. A claim needs to recite active, positive steps delimiting how this use is actually practiced. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

8. Claims 17-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the administration of an effective inhibitory amount of H.pylori thioredoxin to cells and mammals for inhibiting NF-kB activity that is transcriptionally activated, does not reasonably provide enablement for the prevention or treatment of any inflammatory disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant Specification describes an isolated H.pylori thioredoxin protein that has redox activity and ability to inhibit NF-kB activity associated with inflammation [0009] when the protein contains the redox active peptide sequence CGPC, in an in vitro cell culture based system when present in an effective inhibitory amount [0027]. The in vitro assay data was determined to suggest that H. pylori thioredoxin has in vivo potential therapeutic utility. The specification fails to teach how to formulate and use the claimed H.pylori thioredoxin protein, and any H.pylori thioredoxin derivatives, fragments that do not comprise the critical active site or variants which evidence any amino acid sequence or biological activity to treat or prevent any and all inflammatory conditions, to include HIV associated autoimmune disease (instant claim 22 “or other autoimmune diseases”) through administration of any amount, by any route of

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administration to any subject ^{for} for the purpose of obtaining a vaccine effect ~~of~~ prevention or treatment of an inflammatory condition.

The term "vaccine" encompasses the ability of the specific protein, and in this case H.pylori thioredoxin protein, variants, fragments and derivatives of the protein, to induce and/or produce a protective immune effect. The specification suggests that the H.pylori thioredoxin protein may have therapeutic potential in the prevention and treatment of inflammatory conditions, to include any type of autoimmune disease or chronic disease.

The specification does not provide substantive evidence that the claimed vaccines that comprise any amount of H.pylori thioredoxin protein, protein fragment, derivative or variant thereof to be capable of inducing protective immunity and to achieve prevention of any inflammatory condition, or to treat any type of inflammatory condition through administration of the composition by any route, to any subject. This demonstration is required for the skilled artisan to be able to use the claimed vaccines for their intended purpose of preventing or treating any inflammatory condition. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed vaccines, i.e. would not be able to accurately predict if protective immunity has been induced. In support of the examiner's position, US PG-Pub 2003/0235588 Richon et al is being cited to show thioredoxin to mediate diseases and conditions where it is present in elevated amounts (see abstract) and the elevated levels are associated with progression of inflammatory disease (see last four lines of abstract).

Administration of thioredoxin to a subject that already has elevated thioredoxin levels would not serve to prevent or treat any inflammatory condition, but would mediate the continuation or cause the onset of an undesirable condition through increasing the level of thioredoxin in the subject (see Richon et al, page 1, [0003-0010 "heart disease", "chronic and/or

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malignant liver diseases”, “hepatitis C virus infection”, “implicated in various inflammatory and autoimmune diseases”)).

The ability to reasonably predict the capacity of any amount of H.pylori thioredoxin, or any variant, derivative or fragment to induce protective immunity from in vitro studies is problematic in light of the ^{teachings}~~teaches~~ of the prior art that thioredoxin levels are associated with the onset of or continuance of inflammatory or chronic disease conditions. Accordingly, the art indicates that it would require undue experimentation to formulate and use any thioredoxin variant, fragment, or derivative, or even the complete H.pylori thioredoxin as a successful vaccine without the prior demonstration of vaccine efficacy.

The specification fails to teach where or how many mutations can be made to H.pylori thioredoxin to produce a variant or derivative with the claimed functional characteristics of being able to prevent or treat any inflammatory condition or chronic disease.

Further, the specification fails to provide an adequate written description of how any fragment, variant fragment, derivative fragment or mutant fragment can be used to treat or prevent any inflammatory disease or condition, the skilled artisan would be required to de novo locate, identify and characterize the claimed variants, mutants and derivatives of the recited functional characteristics. This would require undue experimentation given the fact that the specification is completely lacking in teachings where in the disclosed H.pylori thioredoxin protein single or multiple changes would or could be tolerated and result in a variant, fragment or derivative with the claimed characteristics. The instant claimed invention is enabled for a scope of what is now claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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9. Claims 19-24 recite the limitations "inflammatory bowel disease", "rheumatoid/ autoimmune arthritis", "any chronic disease (claims 21 and 24)", "any one or more diseases", "soft tissue injury", in an effort to further limit the methods step of administering recited in claim 17. There is insufficient antecedent basis for these limitations in claim 17.

10. New Claim 22 recites the phrase "or other autoimmune diseases"; what diseases are being claimed is not positively recited in the claims. Claim 22 is unclear for reciting a ^{phrase} phrase analogous to the term "such as", by reciting the phrase "or other autoimmune diseases".

11. Claim 17 and dependent claims 18-26 recite the indefinite article "a" and correspondence between the recited intended use and the recited methods step is not clearly set forth through the recitation of the indefinite article "a".

12.

Claim Rejections - 35 USC § 102

Please Note: Based upon Applicant's definition provided in the instant Specification at page 3, lines 5-13 which defines the H.pylori derivative, mutant or fragment to include thioredoxins obtained from any prokaryote or eukaryote (see page 3, line 9), but must include the active peptide sequence CGPC (4 or more amino acids), the following prior art rejection is being made of record over the newly submitted claims.

13. Claims 17-26 are rejected under 35 U.S.C. 102(b) as being anticipated by White et al (US Pat. 5,985,261, reference of record).

White et al disclose the instantly claimed invention directed to a method of treating an inflammation (see col. 19-22, claims 1-37; asthma and lung disease (claim 2), cellular injury due to oxidative damage, see '261, col. 22, claim 30), the method comprising the step of:

administering a derivative or fragment or variant of an isolated H.pylori thioredoxin protein (see White et al, col. 22, claims 30-32), which comprises SEQ ID NO 2 "CGPC" to a subject. The recited intended use of the instantly claimed methods does not define over the applied prior art that discloses the recited methods step of administering to a subject a composition that comprises a thioredoxin active site (SEQ ID NO 2 CGPC) containing

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thioredoxin derivative, mutant or fragment of the isolated H.pylori isolated thioredoxin protein.

The instant specification defines the sequence CGPC to confer upon the thioredoxin protein the functional ability to have an effect on NF-KB activity. The reference inherently anticipates the instantly claimed invention as now claimed

1. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594
2. Inherently the reference anticipates the now claimed invention. *Atlas Powder Co. V IRECA*, 51 USPQ2d 1943, (FED Cir. 1999) states "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art.

Conclusion

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

15. Canbreal Therodiagnostics: WO00/59534 discloses the instantly claimed invention directed to preventing or reducing inflammation in a subject through administering an isolated H. pylori thioredoxin protein derivative, fragment or variant, the thioredoxin being administered to HIV infected subjects to help prevent infectivity towards T-lymphocytes (see WO00', page 9, lines 8-12 and pages 30-31, claims 17-19, 22-24) through inhibiting the activity of es-LAPase.

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16. EP 0237189 is cited to show the therapeutic administration of a thioredoxin composition to a subject to reduce an inflammatory response (see title, abstract, col. 1, paragraph 2, col. 2, lines 29-43; col. 3, lines 25-53, col. 6, lines 1-18)

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

1. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
May 22, 2005


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